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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/587,682

07/28/2006

Wei Han

21515YP

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210 7590 12/11/2008  
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EXAMINER

RAHMANI, NILOOFAR

ART UNIT

PAPER NUMBER

1625

MAIL DATE

DELIVERY MODE

12/11/2008

PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/587,682	<b>Applicant(s)</b> HAN ET AL.	
	<b>Examiner</b> NILOOFAR RAHMANI	<b>Art Unit</b> 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on remark dated on 08/21/2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-3,9-11 and 16-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) 1-3,9 and 16-21 is/are allowed.
- 6) ☒ Claim(s) 10 and 11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____                                      |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date <u>08/21/2008</u> .  | 6) <input type="checkbox"/> Other: _____                          |

### DETAILED ACTION

1. Claims 1-3, 9-11, 16-21 are pending and claims 4-8, 12-15 are cancelled in the instant application.
2. The rejection of claims 1-20 under 102(e) over Miyazaki et al., US 7,211,572 is withdrawn in view of applicant's amendment and argument in paper dated on 08/21/2008.

**3. *Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 10-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for treat and prevent any and all diseases mediated by this receptor. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors include 1) the breadth of the claims, 2) the nature of the invention, 3) the state of the prior art, 4) the level of one of ordinary skill, 5) the level of predictability in the art, 6) the amount of direction provided by the

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inventor, 7) the existence of working examples, and 8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

- 1) The breadth of the claims.
- 2) The nature of the invention,
- 3) The state of the prior art,
- 4) The level of one of ordinary skill,
- 5) The level of predictability in the art,
- 6) The amount of direction provided by the inventor,
- 7) The existence of working examples,
- 8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

**The nature of the invention:** The instant invention is drawn to method of inhibiting HIV integrase or a method for treating or preventing infection by HIV or for preventing, treating or delaying the onset of AIDS in a subject in need thereof which comprises administering to the subject an effective amount of the compound according to claim 20.

**The state of the prior art:** “ At the time that the invention was made, the scientific literature tends to show the speculative role of the integrase receptor and its role in the treatment of HIV or AIDS. “In this study, several common plant RIPs including agrostin, gelonin, luffin, alpha-momorcharin, beta-momorcharin, saporin and trichosanthin were examined for the ability to interfere with HIV-1 replication in a variety of mechanistic assays in vitro. These assays included the CD4/gp120 interaction assay, HIV-1reverse transcriptase (RT) assay, HIV-1

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protease assay and HIV-1 integrase assay. The results from this study suggest that the anti-HIV property of RIPs may be due to inhibition of HIV-1 integrase.” (Emphasis added). Collins et al., FEBS letters, (2000 Apr 14) Vol. 471, No. 2-3, pp. 169-72.

**The predictability in the art:** It is noted that the pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. *In re Fisher*, 427 F. 2d 833, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. In the instant case, the instantly claimed invention is highly unpredictable since one skilled in the art would recognize that in regards to the therapeutic effects, whether or not the compounds of formula of claim 1 would be useful for treating a pharmacological condition in a subject.

**Amount of guidance/working examples:** Applicant provides no examples of the test compounds to treat HIV or delaying the onset of AIDS. However, There is no guidance for using a therapeutically effective amount of a compound of Formula (I) could treat any and all HIVdisease. Nor does applicant identify what diseases are treatable by therapeutically effective amount of a compound of Formula (I).

**The breadth of the claims:** The breadth of claims is drawn to method of inhibiting HIV integrase or a method for treating or preventing infection by HIV or for preventing, treating or delaying the inset of AIDS in a subject in need thereof

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which comprises administering to the subject an effective amount of the compound according to claim 20.

**The quantity of undue experimentation needed:** Since the guidance and teaching provided by the specification is insufficient for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, one of ordinary skill in the art, even with high level of skill, is unable to use the instant compounds as claimed without undue experimentation.

**The level of the skill in the art:** The level of skill in the art is high. However, due to the unpredictability in the pharmaceutical art, it is noted that each embodiment of the invention is required to be individually assessed for physiological activity by in vitro and in vivo screening to determine which compounds exhibit the desired pharmacological activity and which diseases would benefit from this activity.

Taking all of the above into consideration, it is not seen where the instant claims 10-11, for treating diseases associated with therapeutically effective amount of a compound of Formula (I) is efficacious, have been enabled by the instant specification.

4. Further, applicants are not enabled for preventing any of these diseases. The only established prophylactics are vaccines not the compounds such as present here. In addition, it is presumed that "prevention" of the claimed diseases would require a method of identifying those individuals who will develop

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the claimed diseases before they exhibit symptoms. There is no evidence of record that would guide the skilled clinician to identify those who have the potential of becoming afflicted.

“The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art, and the breadth of the claims”, *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. 1) As discussed above, preventing diseases requires identifying those patients who will acquire the disease before occurs. This would require extensive and potentially opened ended clinical research on healthy subjects. 2) The passage spanning line 31, page 39 to line 32, page 40 lists the diseases Applicant intend to treat. 3) There is no working example of such a preventive procedure in man or animal in the specification. 4) The claims rejected are drawn to medical treatment and are therefore physiological in nature. 5) The state of the art is that no general procedure is art-recognized for determining which patients generally will become afflicted before the fact. 6) The artisan using Applicants invention would be a Board Certified physician who specialized to treat diseases with an MD degree and several years of experience. Despite intensive efforts, pharmaceutical science has been unable to find a way of getting a compound to be effective for the prevention of disorder diseases

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generally. Under such circumstances, it is proper for the PTO to require evidence that such an unprecedented feat has actually been accomplished, *In re Ferens*, 163 USPQ 609. No such evidence has been presented in this case. The failure of skilled scientists to achieve a goal is substantial evidence that achieving such a goal is beyond the skill of practitioners in that art, *Genentech vs. Novo Nordisk*, 42 USPQ2d 1001, 1006. This establishes that it is not reasonable to any agent to be able to prevent disorders generally. That is, the skill is so low that no compound effective generally against disorders has ever been found let alone one that can prevent such conditions. 7) It is well established that "the scope of enablement varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). 8) The claims broadly read on all patients, not just those undergoing therapy for the claimed diseases and on the multitude of compounds embraced by Formula (I).

The Examiner suggests deletion of the word "prevention".

**5. Allowable Subject Matter**

Claims 1-3, 9, 16-21 are patentable over Miyazaki et al., US 7,211,572.

The 102(e) rejection is withdrawn due to applicants argument in paper dated on 08/21/2008. Therefore, the claims are free of prior art.

**6.** Any inquiry concerning this communication or earlier communications from the examiner should be directed to Niloofar Rahmani whose telephone number is



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571-272-4329. The examiner can normally be reached on Monday through Friday from 8:30 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres, can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/NILOOFAR RAHMANI/

12/05/2008

/D. Margaret Seaman/

Primary Examiner, Art Unit 1625